A study completed last year of women with early-stage breast cancer found that surgeons no longer universally remove most of the lymph nodes in the underarm area when a biopsy of the nearby lymph nodes shows cancer—a major change in breast cancer management. The study, which evaluated data from 2.7 million U.S. breast cancer patients, was published as in the Journal of the American College of Surgeons.

Until then, it was unclear to what extent surgeons were following the recommendations of a landmark clinical trial published more than four years ago, known as the American College of Surgeons Oncology Group Z-11 trial. Those researchers reported that most early-stage breast cancer patients with tumor in their sentinel lymph node (the first draining node) who underwent lumpectomy do not benefit from surgical removal of the remaining lymph nodes in the underarm area, called completion axillary lymph node dissection (ALND). That study found no difference in cancer recurrence and five-year survival between patients who underwent ALND and those who did not but were monitored for recurrences.

The study found a dramatic increase in the proportion of lumpectomy patients who underwent only a sentinel lymph node biopsy (SNB)—removal of the “gatekeeper” lymph nodes that the cancer is most likely to spread to first—without an ALND after discovery of cancerous sentinel nodes. According to the study authors, the SNB-alone rate more than doubled, from 23 percent in 2009, before publication of the first results1 of the ACOSOG Z-11 trial, to 56 percent in 2011, the most recent data at the time of the study. Because the Z-11 trial results were new in 2011, Dr. Yao said she expects the rate will have increased further in 2012.

Statistical analyses revealed that lumpectomy patients were more likely to undergo ALND if they had any of the following characteristics considered high risk: age younger than 50; black race; triple negative tumors (absence of the three most common types of receptors known to fuel most breast cancer growth); and larger tumors (3 cm or less). In addition, patients with two positive sentinel lymph nodes were twice as likely to have an ALND as patients with one tumor-positive sentinel node. Patients whose tumor metastases measured 2 mm (the width of two grains of rice) or larger were more than three times likelier to undergo ALND compared with patients who had a smaller spread of the cancer, called micrometastases.

Dr. Yao said her findings suggest that some practitioners may feel uncomfortable not performing ALND in high-risk patients, although the Z-11 trial included them. She called for more education for surgeons regarding the applicability of the Z-11 trial findings to these high-risk subgroups and for longer follow-up of these high-risk patients.

The researchers also analyzed 400,052 breast cancer cases that did not meet one of the Z-11 trial’s eligibility criteria for having SNB alone. These patients underwent lumpectomy and radiation therapy to the whole breast; had tumors 5 centimeters or smaller (less than 2 inches) that appeared clinically node negative; had negative surgical margins (no cancer cells were at the outer edge of the breast tissue removed); and had two or fewer tumor-positive sentinel lymph nodes.

The rate of SNB alone reportedly increased from 6.1 percent in 1998 to 56 percent in 2011, the most recent data at the time of the study. Because the Z-11 trial results were new in 2011, Dr. Yao said she expects the rate will have increased further in 2012.

For the study, Dr. Yao and colleagues used the National Cancer Data Base (NCDB), a joint project of the American College of Surgeons Commission on Cancer (CoC) and the American Cancer Society. NCDB captures an estimated 70 percent of newly diagnosed cancer cases in the United States from approximately 1,500 cancer programs accredited by the CoC.

Although NCDB does not identify the type of lymph node dissection (SNB or SNB plus ALND) performed, the researchers used the number of lymph nodes removed as surrogates for these procedures. They categorized the removal of four or fewer lymph nodes as SNB only and removal of 10 or more nodes as ALND.

From the 2.72 million breast cancer cases diagnosed between 1998 and 2011 and listed in the database, the investigators found that 74,399 patients met the Z-11 trial’s eligibility criteria for having SNB alone. These patients underwent lumpectomy and radiation therapy to the whole breast; had tumors 5 centimeters or smaller (less than 2 inches) that appeared clinically node negative; had negative surgical margins (no cancer cells were at the outer edge of the breast tissue removed); and had two or fewer tumor-positive sentinel lymph nodes.

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The researchers also analyzed 400,052 breast cancer cases that did not meet one of the Z-11 trial’s eligibility criteria. Dr. Yao said these results were “somewhat surprising.” They reported that more than 22 percent of patients who underwent a mastectomy in 2011 had only SNB despite mastectomy patients not being included in the Z-11 trial. In addition, SNB without ALNB occurred in more than 50 percent of patients who had tumors larger than the recommended 5 cm or those who received no or partial radiation therapy, rather than whole-breast irradiation.

“It is a little concerning that patients who fall outside the Z-11 eligibility criteria are getting SNB alone,” Dr. Yao said. “It’s controversial to perform SNB alone in mastectomy patients because we don’t know if it affects overall outcomes.”

Information for this article was provided by the American College of Surgeons.
Study Shows Association Between Breastfeeding and Reduced Risk of Breast Cancer

A large international study shows that breastfeeding is associated with a lower risk of developing an aggressive form of breast cancer called hormone-receptor negative. This new combined evidence shows the risk was reduced by up to 20% in women who breastfed. Published in Annals of Oncology, this breastfeeding meta-analysis is a collaboration between Breastcancer.org; Icahn School of Medicine at Mount Sinai; Washington University, St. Louis; and the American Cancer Society.

Hormone-receptor-negative (HRN) breast cancers are more likely to be aggressive and life-threatening. This subtype is more commonly found among women who have not breastfed. The genomes of 20,000 black women with HRN breast cancers, as are women with the BRCA1 gene mutation. Other factors may put these women at even higher risk for developing HRN breast cancer, including obesity and multiple early pregnancies. Furthermore, women with these multiple risk factors are least likely to breastfeed.

In the United States, HRN breast cancers represent about 20% of all breast cancers. This subtype of breast cancer has no receptors for estrogen, progesterone, or HER2, medications that target hormone-driven breast cancers—such as aromatase inhibitors, hormone reductases, and PI3K inhibitors. Breastfeeding is a relatively accessible, low-cost, short-term strategy that yields long-lasting natural protection.

This work highlights the need for more public health strategies that directly inform women and girls about the maternal and (mental) benefits of breastfeeding before and during a woman's child-bearing years. It's also important for these women to have the message reinforced by their healthcare professionals.

It's critical to remove the barriers to breast-feeding at home, in the community, and in the workplace. "All approaches will be necessary in order to protect the most women against the devastation of breast cancer over their lifetimes," said Farhad Islami, M.D., Ph.D., director of interventions, Surveillance and Health Services Research, American Cancer Society. "Pregnant women and young mothers are especially receptive and motivated to make healthy choices. We need to encourage women who are able to breastfeed to do so for their breast health, in addition to the health of their children," said Paolo Boffetta, M.D., associate director for population sciences at the Icahn School of Medicine at Mount Sinai. "Further prospective research will be necessary to further understand the full impact of breastfeeding duration and its effect on other subtypes."

Information for this article was provided by Breastcancer.org.
There were more than 15.5 million Americans with a history of cancer as of January 1, 2016, a number that is projected to reach more than 20 million by 2026. That's according to Cancer Treatment and Survivorship Statistics, 2016, published in CA: A Cancer Journal for Clinicians, a peer-reviewed journal of the American Cancer Society, and its companion publication for consumers, Cancer Treatment & Survivorship Facts & Figures, 2016-2017. The report was released ahead of National Cancer Survivors Day, Sunday June 5, 2016.

Although overall cancer incidence rates are declining in men and stable in women, the number of cancer survivors continues to increase in the United States because of a growing and aging population, as well as increases in cancer survival because of advances in early detection and treatment.

The report is produced every two years in collaboration with the National Cancer Institute to estimate the numbers of current and future cancer survivors to help the public health community better serve this unique population, many of whom cope with long-term physical effects of treatment as well as psychological and socioeconomic sequelae.

The three most prevalent cancers in 2016 are prostate (3,306,760), colorectal (724,690), and melanoma (614,460) among men and breast (3,560,570), uterine corpus (757,190), and colorectal (727,350) among women. The distribution of prevalent cancers (the number of previously diagnosed cancers among people who are alive) differs from incident cancers (the number of newly diagnosed cancers). For example, lung cancer is the second most commonly diagnosed cancer in men, but ranks eighth in prevalence, largely because of poor survival.

One-third of survivors in the U.S. today were diagnosed less than five years ago and more than one-half (56%) were diagnosed within the past 10 years. Nearly half (47%) are age 70 years or older, although age distribution varies by cancer type. For example, the majority of prostate cancer survivors (64%) are age 70 years or older, compared to just one in three (37%) melanoma survivors. The report estimates that there are 65,190 cancer survivors aged 14 and under and 47,180 aged 15 to 19 years in the United States.

In the article, the term “cancer survivor” is used to describe a person who has a history of cancer, from the time of diagnosis through the remainder of his or her life. It includes patients currently undergoing treatment and those who may have become cancer-free. It is important to note that not all people with a history of cancer identify with the term “cancer survivor.”

“People with a history of cancer have unique medical and psychosocial needs that require proactive assessment and management by primary care providers,” write the authors. “Although there are a growing number of tools that can assist patients, caregivers, and clinicians in navigating the various phases of cancer survivorship, further evidence-based resources are needed to optimize care.”

The report says identification of the best practices for delivering quality posttreatment cancer care is needed and points to ongoing efforts by the American College of Surgeons, the Alliance for Quality Psychosocial Cancer Care, and the American Cancer Society (ACS). The ACS has begun to produce guidelines to assist primary care and other clinicians in the provision of care for people with a history of cancer.

For more information, visit cancer.org.
Uncovering a New Principle in Chemotherapy Resistance in Breast Cancer

A laboratory study has revealed an entirely unexpected process for acquiring drug resistance that bypasses the need to re-establish DNA damage repair in breast cancers that have mutant BRCA1 or BRCA2 genes. The findings, reported by Andre Nussenzweig, Ph.D., and Shyam Shanthy, Ph.D., at the National Cancer Institute (NCI), part of the National Institutes of Health, and colleagues, appeared July 21, 2016, in Nature.

In normal cells, the proteins BRCA1 and BRCA2 act as DNA damage sensors, surveyors, and responders. They help perform complex functions that facilitate the repair of damaged DNA. Individuals who inherit certain mutations in either the BRCA1 or BRCA2 gene have defective DNA repair and an increased risk of developing breast, ovarian, and other cancers. Specifically, mutations in BRCA1 and BRCA2 account for 20 percent to 25 percent of hereditary breast cancers and 5 percent to 10 percent of all breast cancers. The reduced ability to repair breaks in DNA in cells with a BRCA1 or BRCA2 mutation makes the cells sensitive to DNA-damaging drugs. However, breast cancer cells eventually acquire resistance to these drugs. One documented mechanism for developing chemoresistance in such tumor cells is through the restoration of accurate DNA repair pathways that mend DNA breaks caused by chemotherapy. Nussenzweig’s laboratory has spent the past decade trying to understand the cellular mechanisms that regulate DNA repair in normal and pathogenic cells. “It is the intricate mechanism that tumor cells evolve to bypass the need for accurate DNA repair that form the foundation of our study,” said Nussenzweig. “A deeper knowledge of the processes that drive drug resistance in BRCA1/2-mutant tumors will lead to novel therapeutic approaches that target tumor-specific vulnerabilities.”

In this study, the researchers linked the protection and stabilization of DNA replication forks as a major contributory mechanism to drug resistance in BRCA1/2-mutant breast and ovarian cancers. Replication is a cellular process that produces two indistinguishable DNA copies from a single DNA molecule. This DNA-copying process is an essential step in cellular division and occurs at defined locations called replication forks.

The movement of a replication fork as it migrates along a DNA molecule can be disrupted by the presence of a diverse group of DNA structures and proteins, collectively and loosely referred to as replication fork barriers. This interruption of replication fork migration results in what is called a stalled fork. Upon replication fork stalling, the BRCA1 and BRCA2 proteins are called upon to protect the newly synthesized strands of DNA. If these proteins are absent, the replication fork is destabilized and the newly synthesized DNA is degraded, which increases genomic instability and increases sensitivity to DNA-damaging drugs.

The investigators were able to identify other proteins, such as FTO, CHD4, and PARF1, that actively promote replication fork destabilization through the recruitment of enzymes that degrade newly synthesized DNA. The absence of these proteins protected the DNA at replication forks and remarkably reversed the drug sensitivity of both BRCA1- and BRCA2-mutant cells, making them chemosensitive. These studies also highlighted the complex ways by which tumor cells can evade chemotherapeutic interventions and acquire drug resistance, since disrupting the activity of multiple proteins led to the same end point of replication fork protection. These results are of particular relevance in the clinical setting, where expression of these proteins appears to be an indicator of how patients with BRCA1- and BRCA2-mutant cancers will respond to chemotherapeutic treatment with DNA-damaging agents.

All together, these results underscore the importance of replication fork barriers to genomic instability and drug sensitivity in the context of BRCA1/2 mutations. The results also suggest that the cellular levels of these proteins could be used as a prognostic factor in acquired resistance in BRCA1/2-mutant cancers. “Our work is starting to not only refine, but also redefine, the current dogma in the field, which states that restoring DNA repair pathways are the only means by which BRCA1-mutant cells can become chemosensitive,” concluded Nussenzweig.

Information for this article was provided by the National Cancer Institute, which leads the National Cancer Program and the NIH’s efforts to dramatically reduce the prevalence of cancer and improve the lives of cancer patients and their families, through research into prevention and cancer biology, the development of new interventions, and the training and mentoring of new researchers. For more information about cancer, please visit the NCI2 website at www.cancer.gov.

New American Cancer Society Breast Cancer Book Offers Hope for the Recently Diagnosed

The American Cancer Society last month unveiled the publication Breast Cancer Clear & Simple, Second Edition: All Your Questions Answered, an engaging, question-and-answer book written to help newly diagnosed patients quickly digest the crucial information needed to navigate through their breast cancer experience.

Breast Cancer Clear & Simple was written to help women with breast cancer and their caregivers know what to expect, what to do, and how to get through what can be an overwhelming, life-changing experience. Professional illustrations throughout the book can help patients understand how breast cancer starts in the body, facts about breast anatomy, the lymph system, and the types of breast reconstruction available.

“When women are diagnosed with breast cancer, they have a lot to think about and a seemingly endless amount of decisions to make. This book supports them by providing a comprehensive and easy-to-understand format to help them navigate through their diagnosis and treatment options, especially during those first days and months,” said Dr. Richard Wender, chief cancer control officer, American Cancer Society.

Written by medical experts from the American Cancer Society, with guidance from breast cancer survivors, this evidence-based book is a great resource for any breast cancer patient. “This book is an important and innovative tool to support patients with a breast cancer diagnosis to help them make the treatment choices that are right for them,” said Dr. J. Leonard Lichtenfeld, deputy chief medical officer, American Cancer Society.

Breast cancer remains the most frequently diagnosed cancer in women. This year, invasive breast cancer will be diagnosed in about 246,660 women. An additional 61,000 new cases of in situ breast cancer will be diagnosed. Survival rates are generally higher for women with early-stage cancers.

Breast Cancer Clear & Simple, Second Edition: All Your Questions Answered is available in both print and ebook formats.

To order this book, go to acsbookstore.ipgbook.com. For bulk order requests, email us at trade@cancer.org. For help with your order, call Independent Publishers Group (IPG) at (800) 888-4741.